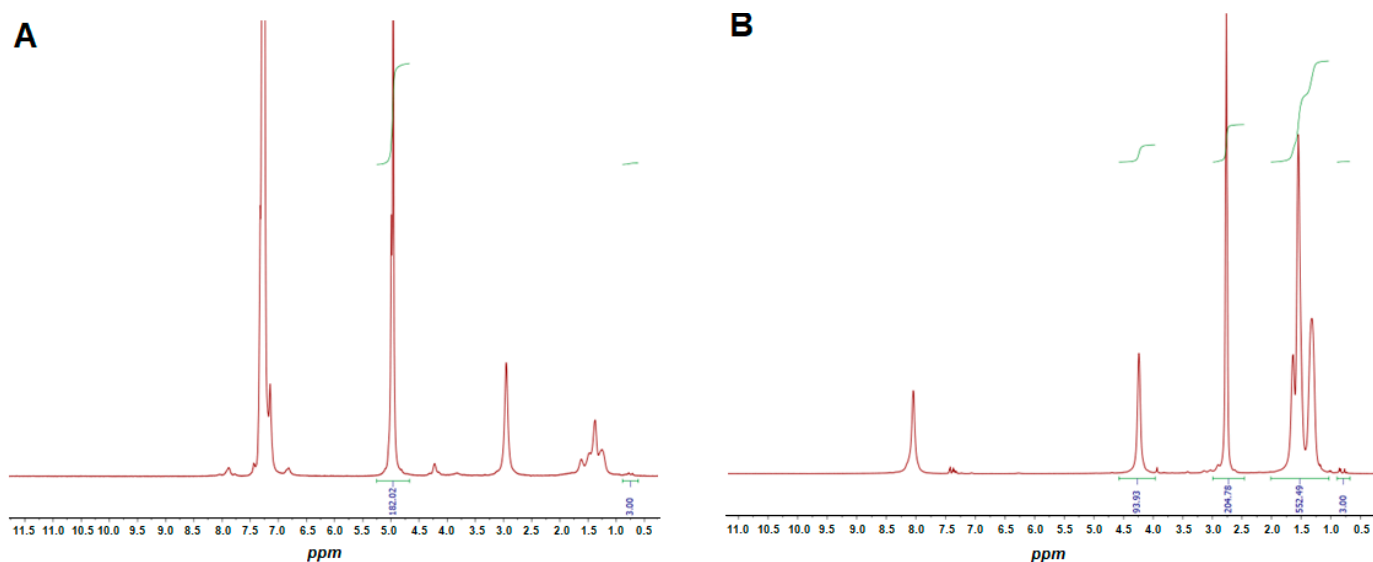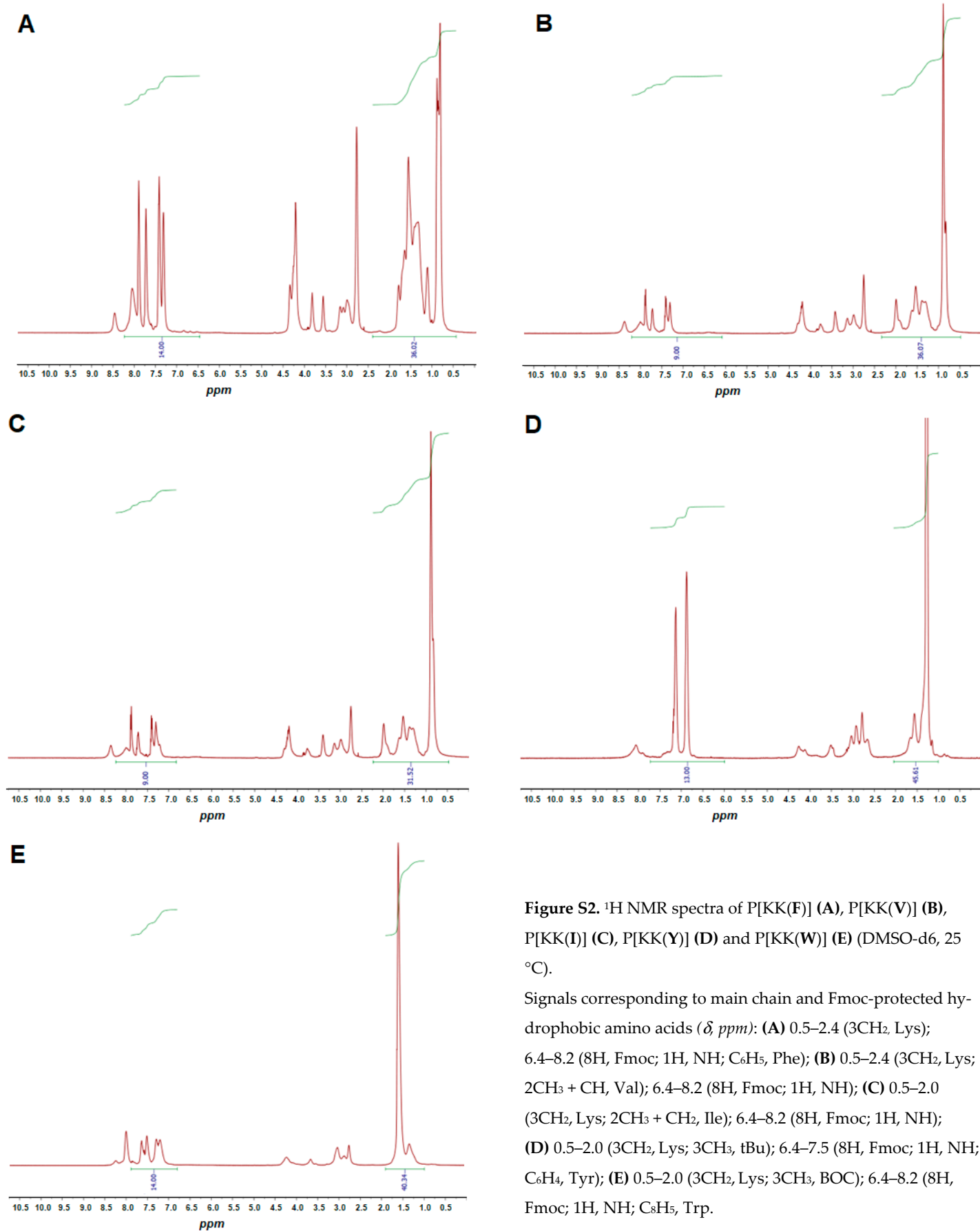*Supplementary Materials*

Amphiphilic Polypeptides Obtained by Post-Polymerization Modification of Poly-L-Lysine as Systems for Combined Delivery of Paclitaxel and siRNA
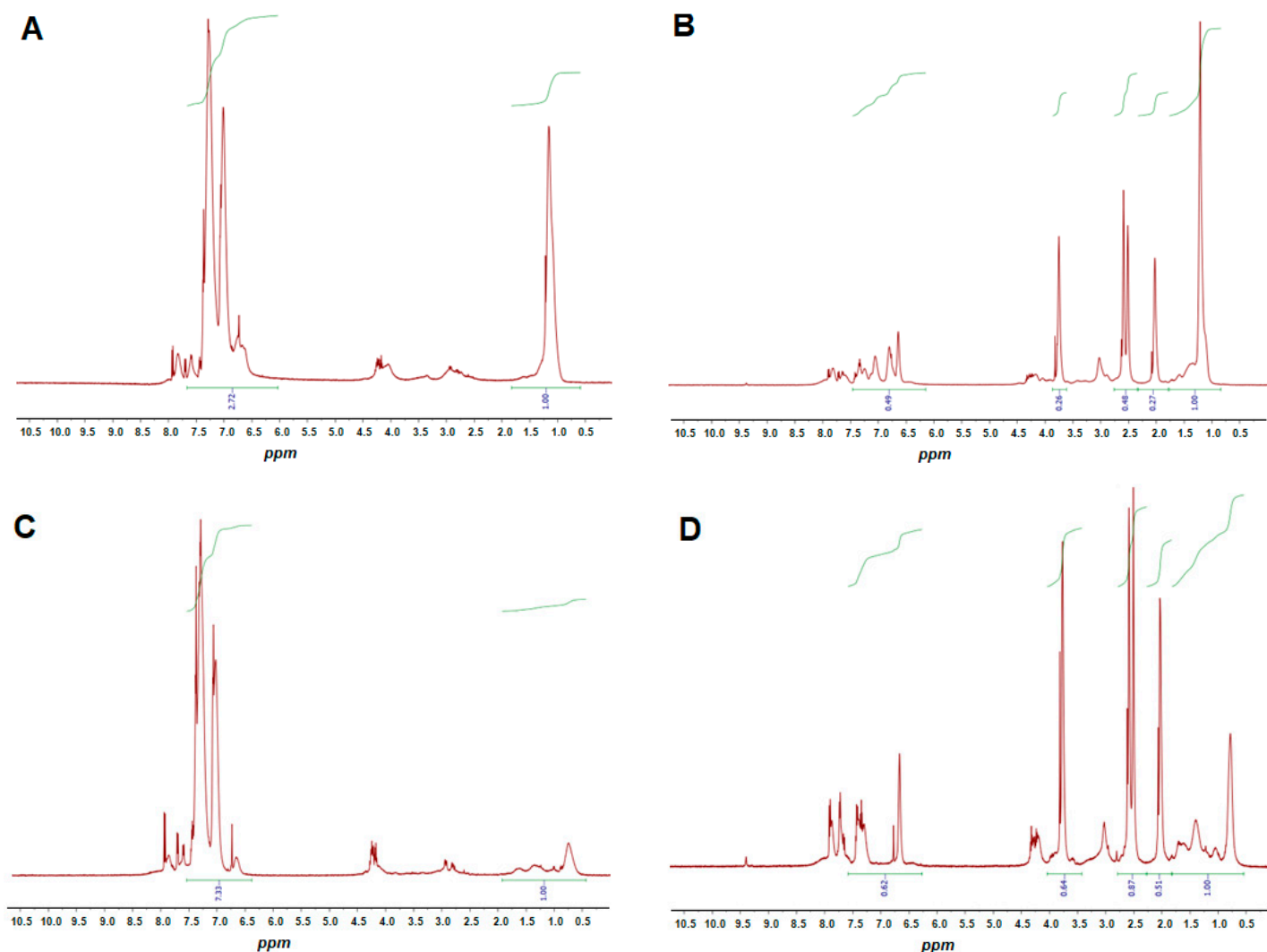
Apollinariia Dzhuzha [1,2], Erik Gandalipov [3], Viktor Korzhikov-Vlakh [1], Elena Katernyuk [1,2], Natalia Zakharova [2], Sergey Silonov [1,4], Tatiana Tennikova [1] and Evgenia Korzhikova-Vlakh [1,2,*]

[1] Institute of Chemistry, Saint-Petersburg State University, Universitetsky Pr. 26, St. Petersburg 198504, Russia; polinadzhuzha@mail.ru (A.D.); v_korzhikov@mail.ru (V.K.-V.); st068478@student.spbu.ru (E.K.); silonovsa25@yandex.ru (S.S.); tennikova@mail.ru (T.T.)

[2] Institute of Macromolecular Compounds, Russian Academy of Sciences, Bolshoy Pr. 31, St. Petersburg 199004, Russia; zakharova@gmail.com

[3] International Institute of Solution Chemistry and Advanced Materials Technologies, ITMO University, Lomonosov Street 9, St. Petersburg 191002, Russia; gandalipov@scamt-itmo.ru

[4] Institute of Cytology, Russian Academy of Sciences, Tihkorezky Pr. 4, St. Petersburg 194064, Russia

* Correspondence: vlakh@hq.macro.ru

* Correspondence: vlakh@hq.macro.ru

Figure S1. ^{1}H NMR spectra of P[K(Z)] (A) and P[K] (B) (DMSO-d6 for (A) and D_2O for (B), 25 °C). In spectra: *(δ, ppm)*: 0.83 (C$\underline{H}_3$, hexylamine), 1.0-2.0 (3C$\underline{H}_2$, Lys), 2.5-3.0 (C$\underline{H}_2$, Lys), 4.0-4.4 (C$\underline{H}$, Lys); 4.7-5.2 (-C$\underline{H}_2$-C_6H_5, Z-group) (A). The degree of polymerization (DP) is 91. Z-group signals are completely absent from the B spectrum, indicating complete deprotection.

A

B

C

D

E

Figure S2. ^{1}H NMR spectra of P[KK(**F**)] **(A)**, P[KK(**V**)] **(B)**, P[KK(**I**)] **(C)**, P[KK(**Y**)] **(D)** and P[KK(**W**)] **(E)** (DMSO-d6, 25 °C).

Signals corresponding to main chain and Fmoc-protected hydrophobic amino acids *(δ, ppm)*: **(A)** 0.5–2.4 (3CH$_2$, Lys); 6.4–8.2 (8H, Fmoc; 1H, NH; C$_6$H$_5$, Phe); **(B)** 0.5–2.4 (3CH$_2$, Lys; 2CH$_3$ + CH, Val); 6.4–8.2 (8H, Fmoc; 1H, NH); **(C)** 0.5–2.0 (3CH$_2$, Lys; 2CH$_3$ + CH$_2$, Ile); 6.4–8.2 (8H, Fmoc; 1H, NH); **(D)** 0.5–2.0 (3CH$_2$, Lys; 3CH$_3$, tBu); 6.4–7.5 (8H, Fmoc; 1H, NH; C$_6$H$_4$, Tyr); **(E)** 0.5–2.0 (3CH$_2$, Lys; 3CH$_3$, BOC); 6.4–8.2 (8H, Fmoc; 1H, NH; C$_8$H$_5$, Trp.

Figure S3. ^{1}H NMR spectra of P[KK(**Y**)K(**H**)] **(A)**, P[KK(**Y**)K(**R**)] **(B)**, P[KK(**I**)K(**H**)] **(C)**, P[KK(**I**)K(**R**)] **(D)** (DMSO-d6, 25 °C). Signals corresponding to main chain and protected amino acids in the side chain *(δ, ppm)*: **(A)** 0.5–2.0 (3CH$_2$, Lys; 3CH$_3$, tBu); 6.4–7.5 (8H, Fmoc; 1H, NH; C$_6$H$_4$, Tyr; 3C$_6$H$_5$, Trt; 2H, His); **(B)** 0.5–1.8 (3CH$_2$, Lys; 3CH$_3$, tBu; 2CH$_2$, Arg); 1.8-2.3 (CH2, Arg); 2.4-2.7 (3CH$_3$, Mtr); 3.5-3.9 (CH$_3$-O, Mtr); 6.4-7.5 (8H, Fmoc; 1H, NH; C$_6$H$_4$, Tyr; H-Ar, Arg); **(C)** 0.5–2.0 (3CH$_2$, Lys; 2CH$_3$ + CH$_2$, Ile); 6.4–8.2 (8H, Fmoc; 1H, NH; 3C$_6$H$_5$, Trt; 2H, His); **(D)** 0.5–1.8 (3CH$_2$, Lys; 2CH$_3$ + CH$_2$, Ile; 2CH$_2$, Arg); 1.8-2.3 (CH2, Arg); 2.4-2.7 (3CH$_3$, Mtr); 3.5-4.0 (CH$_3$-O, Mtr); 6.4-8.2 (8H, Fmoc; 1H, NH; H-Ar, Arg).
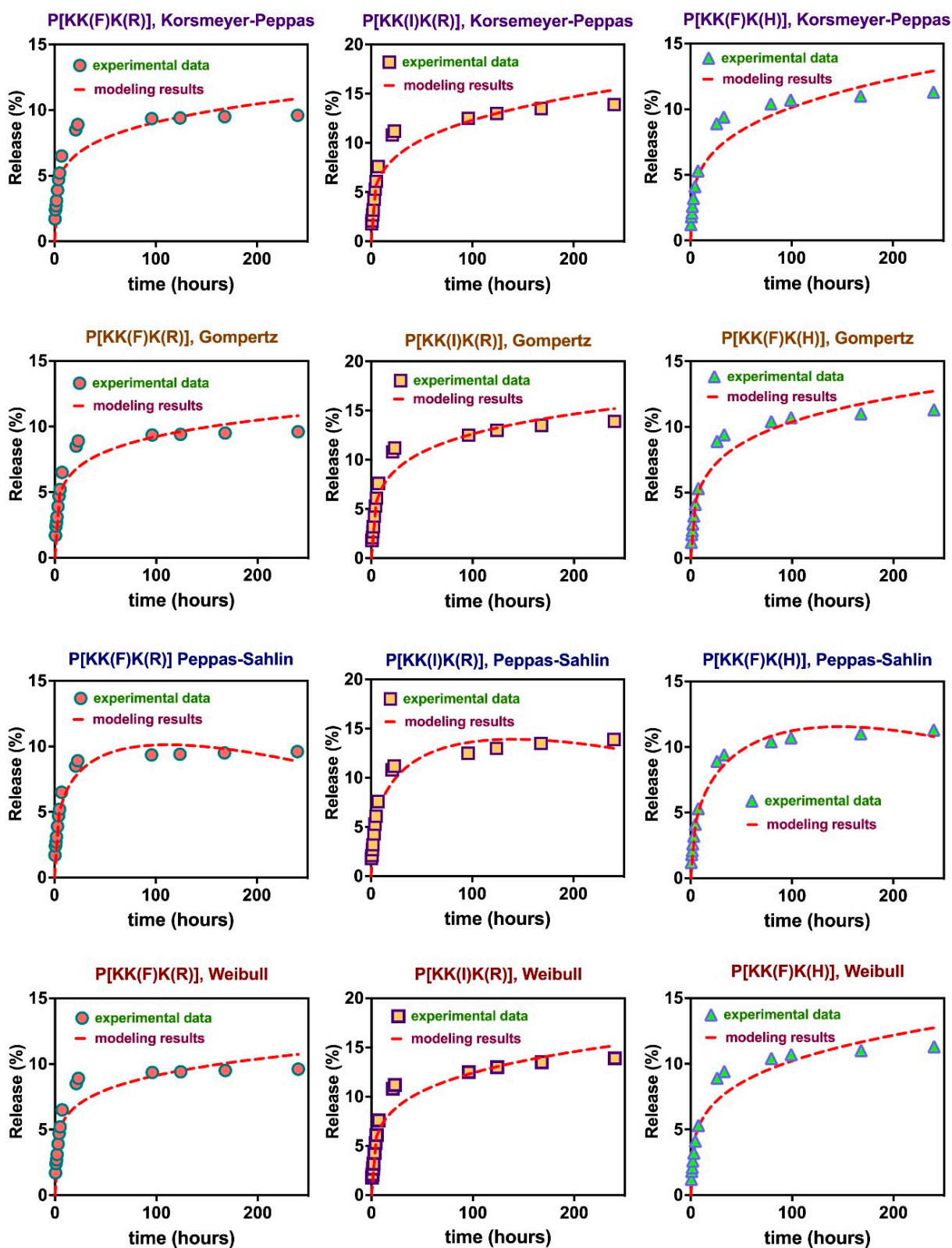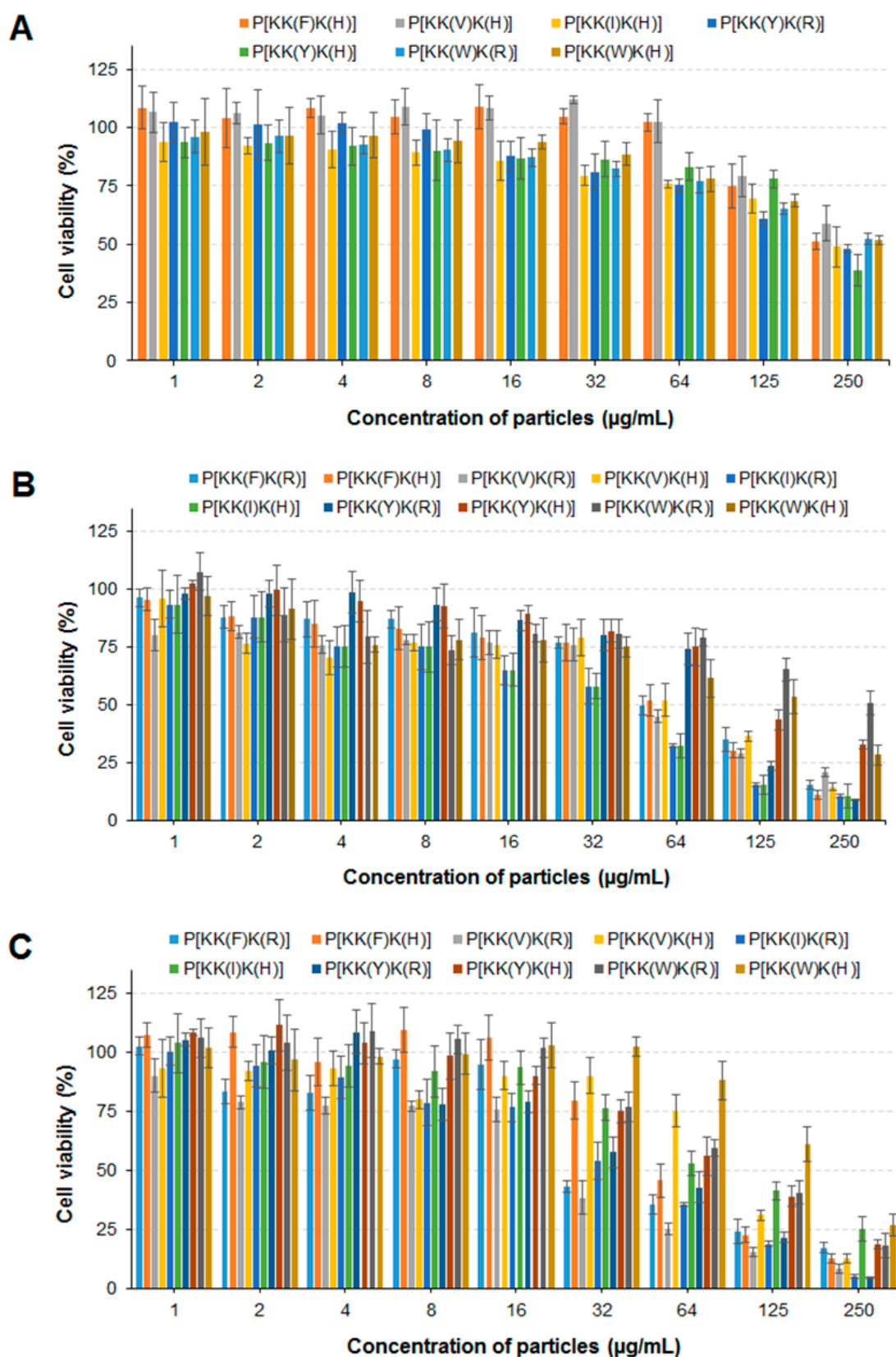
Figure S4. Best model fittings for PTX release from various polypeptide formulations under study.

Table S1. Lipophilicity of some amino acids calculated from experimental results elsewhere.
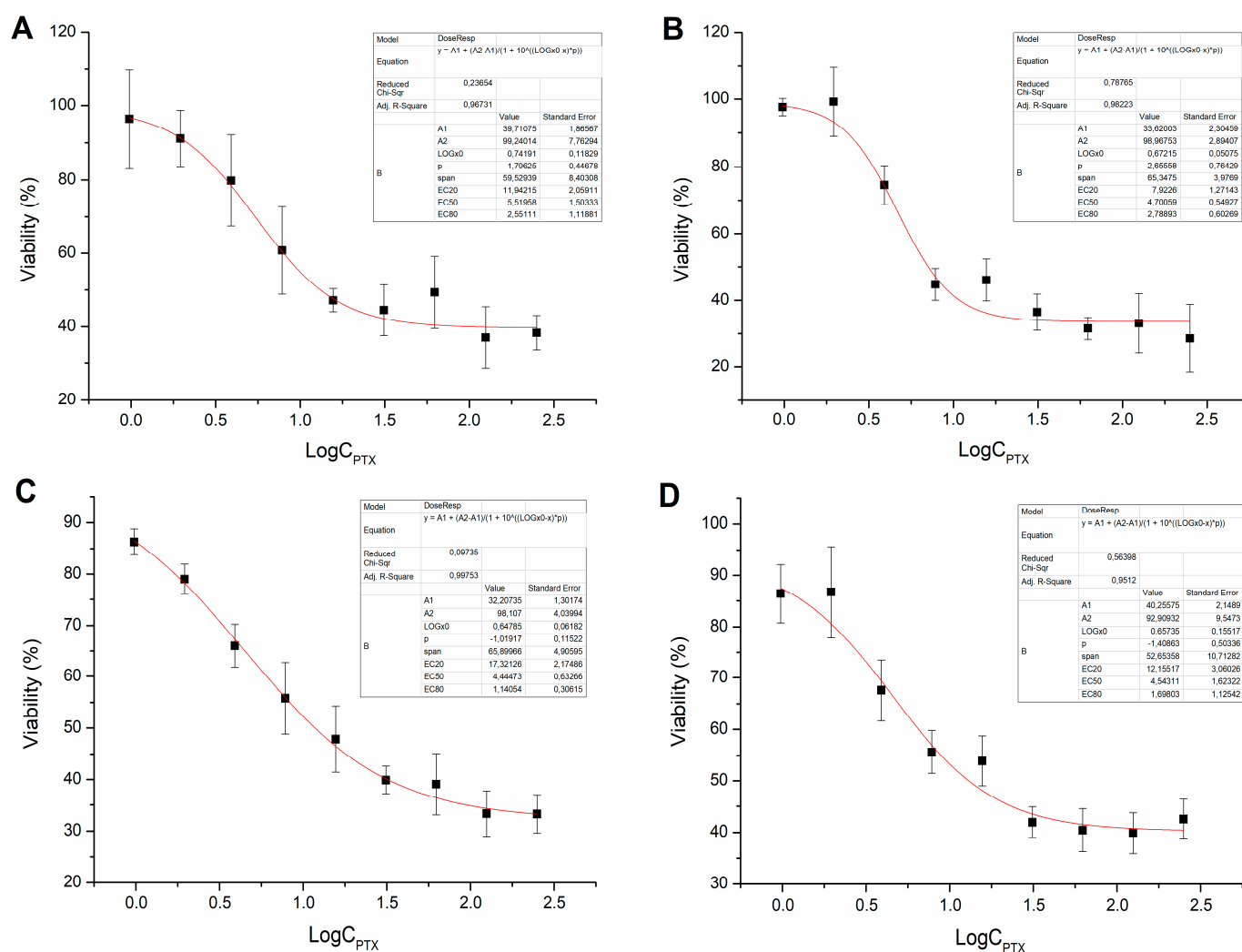
Amino acid	Lipophilicity	
	Parker et al. [1]	**Chmelik et al. [2]**
Tyrosine (Tyr, Y)	1.9	0.85
Valine (Val, V)	3.7	1.07
Isoleucine (Ile, I)	8.0	1.53
Phenylalanine (Phe, F)	9.2	1.91
Tryptophan (Trp, W)	10.0	2.01

References

1.   Parker, J.M.R.; Guo, D.; Hodges, R.S. New hydrophilicity scale derived from high-performance liquid chromatography peptide retention data: correlation of predicted surface residues with antigenicity and x-ray-derived accessible sites. *Biochemistry* **1986**, *25*, 5425–5432.

2.   Chmelík, J.; Hudeček, J.; Putyera, K.; Makovička, J.; Kalous, V.; Chmelíková, J. Characterization of the hydrophobic properties of amino acids on the basis of their partition and distribution coefficients in the 1-octanol-water system. *Collect. Czechoslov. Chem. Commun.* **1991**, *56*, 2030–2041.

Figure S5. Cell viability assay of various polypeptide particles using normal and cancer cells (MTT, 72 h): A – HEK 293T, B – HeLa and C – A549 cell lines.

Figure S6. Dose-response curves for free PTX **(A)** and some its polypeptide formulations **(B-D)**: P[KK(**I**)K(**H**)]@PTX **(B)**, P[KK(**Y**)K(**H**)]@PTX **(C)** and P[KK(**W**)K(**H**)]@PTX **(D)**.